REMARKS

Claims 61-95 and 100 were pending. Claims 64, 69, and 82 have been canceled. Claims 96-99 have been withdrawn. Claims 61-63, 65-68, 70-81, 83-95 and 100 have been amended. Claims 101, 102 and 103 have been added.

Support for the amendments to the claims can be found in the claims as originally filed and at least, for example, at page 15 to page 16. Accordingly, no new matter has been added to the application by way of these amendments.

The foregoing claim amendments have been made solely for the purpose of expediting prosecution of the present application and should in no way be construed as an acquiescence to any of the Examiner's rejections in this or in any former Office Action issued in the present application. Applicants reserve the right to pursue the subject matter of the present claims prior to being amended herein in this application or in another related application.

In view of the foregoing claim amendments and the arguments set forth below, Applicants respectfully submit that the claims are now in condition for allowance.

Objections to the Claims

The objections to the claims at pages 3-4 of the Office Action have been addressed by way of amendment, thereby obviating the objections.

The Pending Claims

The pending claims are directed to compositions comprising a monoclonal antibody or antigen binding fragment thereof-having binding specificity to Lipoteichoic acid (LTA) of Gram positive bacteria and a carrier, wherein the antibody i) binds to both coagulase positive and coagulase negative Staphylococci, ii) enhances opsonization of Gram positive bacteria by phagocytic cells over background as compared to an appropriate control in an in vitro opsonization assay, and iii) confers a statistically significant enhancement of survival or reduces bacteremia in an animal model, wherein the composition is formulated for pharmaceutical administration. The pending claims are further directed to monoclonal antibodies, or antigen binding fragments thereof, having binding specificity to LTA, wherein at least one variable heavy or variable light region of the antibody has at least 70% amino acid identity with at least

one variable heavy or variable light region of the monoclonal antibody 96-110 MAB. Thus, the pending claims are directed to monoclonal antibody compositions having certain functional characteristics or certain structural characteristics, i.e., amino acid sequence identity with the 96-110 monoclonal antibody.

The claimed antibodies were not taught or suggested in the art. At the time the application was filed, anti-techoic acid antibodies that had been identified (in particular, those with binding to both coagulase negative and coagulase positive *Staphylocci*) were found not to be opsonic and not to afford protection against bacteremia or endocarditis. (See the specification as filed at, e.g., pages 11-13 and the references cited therein).

Rejection of Claims 61, 77-79, 92-93 and 95
Under Doctrine of Obviousness-type Double Patenting

The Examiner has rejected claims 61, 77-79, 92-93 and 95 under the judicially created doctrine of obviousness-type double patenting, as being unpatentable over claims 1-7, 9-12 and 14-19 of U.S. Patent No. 6,610,293. Applicants will consider filing a terminal disclaimer over the 6,610,293 patent when the remaining rejections have been overcome.

The Examiner has also provisionally rejected claims 61-93, 95 and 100 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 53-76, 79-83 and 89 of copending Application No. 11/193,440. This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. If appropriate, Applicants will address any obviousness-type double patenting issues upon an indication of allowance of claims in Application No. 11/193,440 or in the instant application.

The Examiner has also provisionally rejected claims 77-88, 92-93 and 95 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7, 9-14, and 17-19 of copending Application No. 10/323,927. Application No. 10/323,927 has now issued as U.S. Patent No. 7,250,494. Applicants respectfully traverse this rejection.

The instant claims are not obvious variations of the claims in U.S. Patent No. 7,250,494 ("the '494 patent"), as is required to support an obviousness-type double patenting rejection. Applicants will consider filing a terminal disclaimer over the 7,250,494 patent when the remaining rejections have been overcome.

The Examiner has also provisionally rejected claims 77-88, 93 and 100 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 40-43, 47-68 and 72 of copending Application No. 10/323,926. This is a *provisional* obviousness-type double

patenting rejection because the conflicting claims have not in fact been patented. If appropriate, Applicants will address any obviousness-type double patenting issues upon an indication of allowance of claims in Application No. 10/323,926 or in the instant application.

Rejection of Claims 77-79, 81-85, 87 and 89-96
Under Section 112, First & Second Paragraphs

The Examiner has rejected claims 77-79, 81-85, 87 and 89-96 under 35 U.S.C. § 112, first and second paragraphs, as failing to comply with the written description requirement and as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention.

Claim 77 has been amended to recite "96-110 MAB," the monoclonal antibody generated from the 96-110 hybridoma, thus obviating the rejections as claims 78, 79, 81-85, 87 and 89-96 depend therefrom. Support for this amendment can be found at least, for example, at page 14 – page 15 of the specification. The sequence of the 96-110 MAB heavy and light chains are shown in SEQ ID NO: 87 and SEQ ID NO:89, respectively.

Claims 61, 69, 88 and 100 were further rejected under §112, second paragraph, as being indefinite in the recitation of the term "fragment thereof."

Without acquiescing and solely in the interest of expediting prosecution, the claims have been amended.

Rejection of Claim 94
Under Section 101 – Non-statutory Subject Matter

The Examiner has rejected claim 94 under §101 for being directed to non-statutory subject matter.

Claim 94 as amended is directed to an antibody composition comprising a monoclonal antibody-having binding specificity to Lipoteichoic acid (LTA) of Gram positive bacteria and a carrier, wherein the antibody i) binds to both coagulase positive and coagulase negative Staphylococci, ii) enhances opsonization of Gram positive bacteria by phagocytic cells over background as compared to an appropriate control in an in vitro opsonization assay, and iii) confers a statistically significant enhancement of survival or reduces bacteremia in an animal model, wherein the composition is formulated for pharmaceutical administration or a monoclonal antibody, or fragments thereof, having binding specificity to LTA, wherein at least one variable heavy or variable light region of the antibody has at least 70% amino acid identity with at least one variable heavy or variable light region of the monoclonal antibody 96-110 MAB and at least

one additional antibody having specificity for LTA, thus obviating the rejection. The amendment to claim 94 obviates the rejection under §101.

Rejection of Claims 61, 62, 64-68, 81, 82, 84-86, 89, 90, 92, 93 and 100 Under Section 102(b)

The Examiner has rejected claims 61, 62, 64-68, 81, 82, 84-86, 89, 90, 92, 93 and 100 under §102(b) as being anticipated by Aasjford *et al.* in light of Roitt *et al.* This rejection is respectfully traversed.

The pending claims are directed to compositions comprising a monoclonal antibody-having binding specificity to Lipoteichoic acid (LTA) of Gram positive bacteria and a carrier, wherein the antibody i) binds to both coagulase positive and coagulase negative Staphylococci, ii) enhances opsonization of Gram positive bacteria by phagocytic cells over background as compared to an appropriate control in an in vitro opsonization assay, and iii) confers a statistically significant enhancement of survival or reduces bacteremia in an animal model, wherein the composition is formulated for pharmaceutical administration. The pending claims are further directed to monoclonal antibodies, or antigen binding fragment thereof, wherein the monoclonal antibody has binding specificity to LTA, wherein at least one heavy chain variable region or light chain variable region of the antibody has at least 70% amino acid identity with at least one heavy or light chain variable region of the monoclonal antibody 96-110 MAB and a carrier.

For the reasons stated below, it is Applicants' position that the Examiner has failed to establish a *prima facie* case of anticipation. "Anticipation requires a showing that each limitation of a claim is found in a single reference, either expressly or inherently." *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1376 (Fed. Cir. 2005). To show that the prior art "necessarily" functions in accordance with, or includes the claimed limitations, one must show more than a mere probability or possibility of the inherent feature's existence. *See SmithKline Beecham Corp. v. Apotex Inc.*, 403 F.3d 1331, 1346 (Fed. Cir. 2005). Therefore, "[i]nherency...may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient." *Mehl/Biophile v.*

Milgraum, M.D., 192 F.3d 1362 at 1365 (emphasis added) (quoting *Hansgirg v. Kemmer*, 102 F.2d 212, 214 (CCPA 1939)).

The Examiner states that Aasjford *et al.* teach anti-lipoteichoic acid (LTA) monoclonal antibodies, which "inherently opsonize gram positive bacteria by 75% over background because...Roitt *et al.* teach antibodies inherently have the ability to opsonize bacteria by virtue of their binding." (p. 16 of 2/23/07 Office Action).

Aasjford discloses two IgM monoclonal antibodies that bind to LTA. The antibodies are not shown to have any of the functional or structural limitations required by the pending claims. Specifically, Aasjford fails to teach or suggest a monoclonal antibody or antigen binding fragment thereof that i) binds to both coagulase positive and coagulase negative Staphylococci, ii) enhances opsonization of Gram positive bacteria by phagocytic cells over background as compared to an appropriate control in an in vitro opsonization assay, and iii) confers a statistically significant enhancement of survival or reduces bacteremia in an animal model, wherein the composition is formulated for pharmaceutical administration. Aasjford also fails to teach or suggest a monoclonal antibody, or antigen binding fragment thereof, wherein the monoclonal antibody has binding specificity to LTA, wherein at least one heavy chain variable region or light chain variable region of the antibody has at least 70% amino acid identity with at least one heavy or light chain variable region of the monoclonal antibody 96-110 MAB and a carrier.

The Roitt et al. reference fails to support the use of the Aasjford reference as an anticipatory piece of prior art. The Examiner's statement that "antibodies inherently have the ability to opsonize bacteria by virtue of their binding" is incorrect with respect to anti-LTA antibodies. In fact, as taught in the instant specification and as known in the art at the time the instant application was filed, anti-techoic acid or anti-LTA antibodies have been reported to lack opsonic activity. Copies of the Fattom et al., Kojima et al., and Takeda et al., references referenced at page 12 of the application as filed are provided herewith as Appendices A – C. These references illustrate that not all antibodies have the claimed functional properties of : i) binding to both coagulase positive and coagulase negative Staphylococci, ii) enhances opsonization of Gram positive bacteria by phagocytic cells over background as compared to an appropriate control in an in vitro opsonization assay, and iii) conferring a statistically significant enhancement of survival or reduces bacteremia in an animal model. Specifically, Takeda et al.

published that antibodies to teichoic acid afforded no protection against bacteremia (Circulation 86(6):2539-2546 (1991); attached as Appendix C). Kojima et al. (Journal of Infectious Diseases 162:435-441 (1990); attached as Appendix B) report similar findings. Further, Fattom *et al.* show that anti-teichoic acid antibodies lacked opsonophagocytic activity (see Figure 2 in J. Clin. Micro. 30(12):3270-3273 (1992); attached as Appendix A). Thus, the claimed functional properties are not inherent in all antibodies. Aasjford *et al.* also fails to teach or suggest a pharmaceutical use for the antibodies disclosed therein, let alone a composition comprising antibodies that bind to LTA formulated for pharmaceutical administration to a neonate.

Aasjford *et al.* also fails to teach or suggest anti-LTA antibodies having structural similarity to the 96-110 MAb as referenced by claim 77 and the claims that depend therefrom.

Accordingly, because Aasjford *et al.*, fails to teach or suggest each and every element of the presently claimed invention with certainty, applicants respectfully request that the rejection under 35 U.S.C. §102(b) be reconsidered and withdrawn.

Rejection of Claims 69-76, 91 and 95
Under Section 102(b)

The Examiner has rejected claims 69-76, 91 and 95 under §102(b) as being anticipated by Takada *et al.* This rejection is respectfully traversed.

The pending claims are directed to compositions comprising a monoclonal antibody having binding specificity to Lipoteichoic acid (LTA) of Gram positive bacteria and a carrier, wherein the antibody i) binds to both coagulase positive and coagulase negative Staphylococci, ii) enhances opsonization of Gram positive bacteria by phagocytic cells over background as compared to an appropriate control in an in vitro opsonization assay, and iii) confers a statistically significant enhancement of survival or reduces bacteremia in an animal model, wherein the composition is formulated for pharmaceutical administration. The pending claims are further directed to monoclonal antibodies, or antigen binding fragment thereof, wherein the monoclonal antibody has binding specificity to LTA, wherein at least one heavy chain variable region or light chain variable region of the antibody has at least 70% amino acid identity with at

least one heavy or light chain variable region of the monoclonal antibody 96-110 MAB and a carrier.

For the reasons stated below, it is Applicants' position that the Examiner has failed to establish a *prima facie* case of anticipation. "Anticipation requires a showing that each limitation of a claim is found in a single reference, either expressly or inherently." *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1376 (Fed. Cir. 2005).

The Examiner states that "Takada *et al.* teaches antigenic reactivity of the LTA extracts from *Enterococcus hirae* with monoclonal antibodies raised against *Streptococcus pyogenes.*" The Examiner further states that Takada *et al.* teach administration of a mixture of saline which is a pharmaceutical carrier, LTA-2, and monoclonal antibody TS-2 injected into MDP-primed C3H/HeN mice" and that "four of the six mice showed complete regression of the established tumors." The Examiner further states that "the strong reactivity of monoclonal antibody TS-2 with the LTA-2 fraction is capable of neutralizing the cytokine inducing activities of the LTA-2 fraction.

First, with respect to the Examiner's characterization of the reference, Applicants point out that, in contrast to the Examiner's statement, regression of the tumors as reported by Takada *et al.,* was due to the injection of the LTA-2 fraction, *not* an anti-LTA monoclonal antibody (see page 61, right column, first paragraph).

The Takada reference discloses a TS-2 monoclonal antibody which can neutralize cytokine-inducing activities of an LTA-2 fraction of *Enterococcus hirae.* The TS-2 antibody was found to neutralize the TNF-alpha and IL-6 inducing activites of LTA-2 in macrophage cultures.

The Takada reference fails to teach or suggest monoclonal antibodies having the claimed functional or structural properties. Specifically, Takada fails to teach or suggest a monoclonal antibody or antigen binding fragment thereof that i) binds to both coagulase positive and coagulase negative Staphylococci, ii) enhances opsonization of Gram positive bacteria by phagocytic cells over background as compared to an appropriate control in an in vitro opsonization assay, and iii) confers a statistically significant enhancement of survival or reduces bacteremia in an animal model, wherein the composition is formulated for pharmaceutical administration. As set forth above, these functional properties were known not to be present in all anti-techoic acid or anti-LTA antibodies. Takeda et al. published that antibodies to teichoic

acid afforded no protection against bacteremia (Circulation 86(6):2539-2546 (1991); attached as Appendix C). Kojima et al. (Journal of Infectious Diseases 162:435-441 (1990); attached as Appendix B) report similar findings. Further, Fattom *et al.* show that anti-teichoic acid antibodies lacked opsonphagocytic activity (see Figure 2 in J. Clin. Micro. 30(12):3270-3273 (1992); attached as Appendix A). Thus, the claimed functional properties are not inherent in all antibodies.

Takada also fails to teach or suggest a monoclonal antibody, or antigen binding fragment thereof, having binding specificity to LTA, wherein at least one variable heavy or variable light region of the antibody has at least 70% amino acid identity with at least one variable heavy or variable light region of the monoclonal antibody 96-110 MAB.

Accordingly, because Takada *et al.*, fails to teach or suggest each and every element of the presently claimed invention with certainty, applicants respectfully request that the rejection under 35 U.S.C. §102(b) be reconsidered and withdrawn.

Rejection of Claim 94
Under Section 102(b)

The Examiner rejects claim 94 under §102(b) as being anticipated by Chugh *et al.* The Examiner also rejects claim 94 under 35 U.S.C. §102(b) as being anticipated by West *et al.*

This rejection is respectfully traversed.

Claim 94 is directed to an antibody composition comprising a monoclonal antibody having binding specificity to Lipoteichoic acid (LTA) of Gram positive bacteria and a carrier, wherein the antibody i) binds to both coagulase positive and coagulase negative Staphylococci, ii) enhances opsonization of Gram positive bacteria by phagocytic cells over background as compared to an appropriate control in an in vitro opsonization assay, iii) confers a statistically significant enhancement of survival or reduces bacteremia in an animal model, wherein the composition is formulated for pharmaceutical administration or a monoclonal antibody, or antigen binding fragment thereof, wherein the monoclonal antibody has binding specificity to LTA, wherein at least one heavy chain variable region or light chain variable region of the antibody has at least 70% amino acid identity with at least one heavy or light chain variable region of the monoclonal antibody 96-110 MAB and a carrier and at least one additional antibody having specificity for LTA.

The Chugh and West references fail to teach or suggest each and every element of the presently claimed invention. Specifically, each of the references fail to teach any monoclonal anti-LTA antibody, let alone any anti-LTA antibody having the claimed funtional or structural properties. Applicants respectfully request that the rejection under 35 USC § 102(b) be reconsidered and withdrawn.

Rejection of Claims 61, 62, 64-67, 81-90, 92, 93 and 100 Under Section 102(b)

The Examiner has rejected claims 61, 62, 64-67, 81-90, 92, 93 and 100 under §102(b) as being anticipated by Hamada *et al.* in light of Roitt *et al.* This rejection is respectfully traversed.

The pending claims are directed to compositions comprising a monoclonal antibody having binding specificity to Lipoteichoic acid (LTA) of Gram positive bacteria and a carrier, wherein the antibody i) binds to both coagulase positive and coagulase negative Staphylococci, ii) enhances opsonization of Gram positive bacteria by phagocytic cells over background as compared to an appropriate control in an in vitro opsonization assay, and iii) confers a statistically significant enhancement of survival or reduces bacteremia in an animal model, wherein the composition is formulated for pharmaceutical administration. The pending claims are further directed to monoclonal antibodies, or antigen binding fragment thereof, wherein the monoclonal antibody has binding specificity to LTA, wherein at least one heavy chain variable region or light chain variable region of the antibody has at least 70% amino acid identity with at least one heavy or light chain variable region of the monoclonal antibody 96-110 MAB and a carrier.

The Hamada reference teaches the anti-LTA monoclonal antibody 3G6. The antibody is not shown to have any of the functional properties set forth in the claims. Furthermore, as set forth above, until the instant invention was made, the claimed properties had been found not to be present in anti-LTA antibodies. Specifically, Takeda et al. published that antibodies to teichoic acid afforded no protection against bacteremia (Circulation 86(6):2539-2546 (1991); attached as Appendix C). Kojima et al. (Journal of Infectious Diseases 162:435-441 (1990); attached as Appendix B) report similar findings. Further, Fattom *et al.* show that anti-teichoic acid antibodies lacked opsonphagocytic activity (see Figure 2 in J. Clin. Micro. 30(12):3270-3273 (1992); attached as Appendix A). Thus, the claimed functional properties are not inherent in all antibodies.

The Hamada et al. reference also fails to teach or suggest a monoclonal antibody having the structural properties required by claim 77 and the claims that depend therefrom.

Accordingly, because Hamada *et al.*, fails to teach or suggest each and every element of the presently claimed invention with certainty, applicants respectfully request that the rejection under 35 U.S.C. §102(b) be reconsidered and withdrawn

Rejection of Claim 94
Under Section 103(a)

The Examiner has rejected claim 94 under §103(a) as being unpatentable over Aasjford *et al.* in view of Hamada *et al.* and in view of Schwarzberg. This rejection is respectfully traversed.

The test for *prima facie* obviousness is consistent with the legal principles enunciated in *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007). *Takeda Chem. Indus., Ltd. v. Alpharma Pty., Ltd.*, 2007 U.S. App. LEXIS 15349, at *13 (Fed. Cir. 2007). "While the *KSR* Court rejected a rigid appliction of the teaching, suggestion, or motivation ("TSM") test, the Court acknowledged the importance of identifying 'a *reason* that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does' in an obviousness determination." *Id.* at *13-14 (quoting *KSR*, 127 S. Ct. at 1731) (emphasis added). Although the TSM test should not be applied in a rigid manner, it can provide helpful insight to an obviousness inquiry. *KSR*, 127 S. Ct. at 1731. The *KSR* Court upheld the secondary considerations of non-obviounsess, noting that there is "no necessary inconsistency between the idea underlying the TSM test and the *Graham* analysis." *Id.* ***Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.*** See M.P.E.P. 2143.

The subject matter of the pending claims is set forth above. As set forth above, Aasjford *et al.* and Hamada *et al.* fail to teach or suggest anti-LTA antibodies having any of the functional or structural limitations required by the pending claims. Schwarzberg fails to make up for this deficiency. The Examiner relies on Schwarzberg for the teaching that fragments retain a high degree of specificity and affinity. However, the only claims that read on fragments of antibodies require a degree of structural similarity to the 96-110 antibody. Antibodies having structural similarity to the 96-110 antibody are not taught or suggested by any of the art of record.

As none of the references, alone or combined, teach an antibody composition comprising a monoclonal antibody-having binding specificity to Lipoteichoic acid (LTA) of Gram positive bacteria and a carrier, wherein the antibody i) binds to both coagulase positive and coagulase negative Staphylococci, ii) enhances opsonization of Gram positive bacteria by phagocytic cells over background as compared to an appropriate control in an in vitro opsonization assay, and iii) confers a statistically significant enhancement of survival or reduces bacteremia in an animal model, wherein the composition is formulated for pharmaceutical administration or a monoclonal antibody, or antigen binding fragment thereof, wherein the monoclonal antibody has binding specificity to LTA, wherein at least one heavy chain variable region or light chain variable region of the antibody has at least 70% amino acid identity with at least one heavy or light chain variable region of the monoclonal antibody 96-110 MAB and a carrier and at least one additional antibody having specificity for LTA, the references fail to teach or suggest all the claim limitations.

In summary, Applicants respectfully request that the rejection of these claims in view of Aasjford *et al.*, Hamada *et al.* and Schwarzberg be reconsidered and withdrawn on the grounds that the references do not teach or suggest each and every element of the claimed invention.

Rejection of Claim 95
Under Section 103(a)

The Examiner has rejected claim 95 under §103(a) as being unpatentable over Takada *et al.* in view of Hamada *et al.* This rejection is respectfully traversed.

Claim 95 is directed to a pharmaceutical composition comprising an effective amount of an antibody of claim 77, for use in a human neonate. Claim 77 requires that the antibody has at least one heavy chain variable region or light chain variable region of the antibody has at least 70% amino acid identity with at least one heavy or light chain variable region of the monoclonal antibody 96-110 MAB

As set forth above, Takada *et al.* and Hamada *et al.* fail to teach or suggest an antibody having the required degree of structural similarity to the 96-110 antibody.

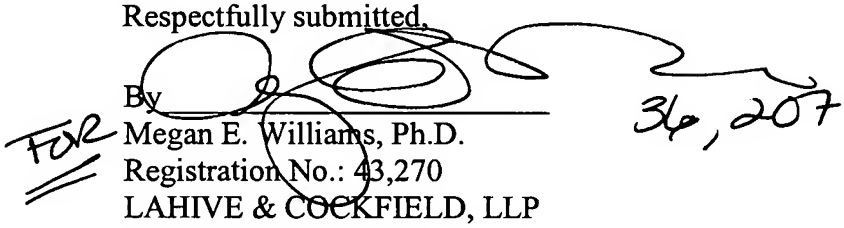
As the references fail to teach or suggest all of the claim limitations, Applicants respectfully request that the rejection of claim 95 be reconsidered and withdrawn.

SUMMARY

If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' Attorney at (617) 227-7400.

Dated: August 23, 2007

Respectfully submitted,



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